Journal of Psychopharmacology
http://jop.sagepub.com/

Salvia divinorum use and phenomenology: results from an online survey

HR Sumnall, F Measham, SD Brandt and JC Cole

J Psychopharmacol 2011 25: 1496 originally published online 11 October 2010
DOI: 10.1177/0269881110385596

The online version of this article can be found at:
http://jop.sagepub.com/content/25/11/1496

Published by:
SAGE
http://www.sagepublications.com

On behalf of:

British Association for Psychopharmacology

Original Paper

Salvia divinorum use and phenomenology: results from an online survey

Psychopharm

Journal of Psychopharmacology
25(11) 1496–1507

DOI: 10.1177/0269881110385596
jop.sagepub.com
SAGE

HR Sumnall[1], F Measham[2], SD Brandt[3] and JC Cole[4]

Abstract

Salvia divinorum is a hallucinogenic plant with ethnopharmacological and recreational uses. It differs from classic serotonergic hallucinogens such as LSD and psilocin in both phenomenology and potent agonist activity of the active component salvinorin A at κ-opioid receptors. Awareness of *S. divinorum* has grown recently, with both an increase in its public representation and concern over its potential harmful effects. This discussion is particularly relevant as *S. divinorum* is legal to use in many countries and regions and easily available through online retailers. Drawing upon previous investigations of *S. divinorum* and other hallucinogens, this study surveyed 154 recent users and questioned them on their use behaviours, consequences of use and other attitudinal measures. Although reporting an extensive substance use history, and considering the limitations of online surveys, there was little evidence of dysfunctional *S. divinorum* use, and few reports of troubling adverse consequences of use. Furthermore, there was no evidence that users exhibited increased schizotypy. Respondents reported that *S. divinorum* produced mixed hallucinogenic and dissociative effects, which lends support to assertions that it phenomenologically differs from other hallucinogens with primary serotonergic activity. The functions of use changed with greater experiences with the drug, and although many respondents reported use of *S. divinorum* as an alternative to illegal drugs it, was apparent that legal proscription would be unlikely to dissuade them from use. These results are discussed with reference to psychopharmacologically informed public health responses to substance use.

Keywords

Drug effects, hallucinogens, *Salvia divinorum*, subjective experiences

Introduction

Salvia divinorum (S. divinorum) has traditional uses as an entheogen and as an ethnopharmacological treatment (Ott, 1995), although it is better known in the developed world as a recreational hallucinogen (Khey et al., 2008). The active component salvinorin A is a potent neoclerodane diterpene hallucinogen with selective agonist activity at κ-opioid receptors (and peripheral actions on cholinergic transmission), distinguishing it from the classic serotonergic hallucinogens such as LSD and psilocin (see Butelman et al., 2007; Capasso et al., 2006; Ortega et al., 1982; Roth et al., 2002). Further indirect actions on dopaminergic, noradrenergic, and endocannabinoid systems have also been characterized (Braida et al., 2008, Grilli et al., 2009; Zhang et al., 2005). The drug is active in humans in doses around 200 μg when administered through vaporization (thus avoiding hepatic first-pass metabolism), and is orally active when held in the mouth for >10 min (Siebert, 1994). One interesting feature of salvinorin A and its naturally occurring derivatives is the lack of nitrogen, and it would appear that none of the currently identified plant constituents are alkaloids. Other compounds isolated from the plant include Salvinorins B–I (Lee et al., 2005; Munro and Rizzacasa 2003; Shirota et al., 2006; Valdés et al., 1984, 2001), divinorin F, salvidivins A–D (Shirota et al., 2006), divinatorins A–F (Bigham et al., 2003; Munro and Rizzacasa, 2003) and salvinicins A and B (Harding et al., 2005). Little is known about whether they would be centrally active in humans, but the salvinorin A nucleus provides a structural template for a large number of chemically altered entities (for example, see Beguin et al., 2006, 2008, 2009). 2-Methoxymethyl-salvinorin B, for example, is a more potent κ-opioid receptor agonist than salvinorin A, and shows longer-lasting behavioural activity in murine tests of ambulation and nociception (Wang et al., 2008).

To date there have been only a few national estimates of *S. divinorum* use prevalence in the general population. In the USA, the National Survey on Drug Use and Health estimated that about 1.8 million persons aged 12 or older used

[1]Centre for Public Health, Liverpool John Moores University, Liverpool, UK.
[2]Department of Applied Social Science, Lancaster University, Lancaster, UK.
[3]School of Pharmacy and Biomolecular Sciences, Liverpool John Moores University, Liverpool, UK.
[4]School of Psychology, University of Liverpool, Liverpool, UK.

Corresponding author:
Dr Harry Sumnall, Centre for Public Health, Liverpool John Moores University, Henry Cotton Building, Webster Street, Liverpool L3 2ET, UK
Email: h.sumnall@ljmu.ac.uk

S. divinorum in their lifetime, and approximately 750,000 did so in the previous year (SAMHSA, 2008). Other local and population-specific studies have been conducted. For example, lifetime prevalence was estimated to be 28.7% and last-year prevalence of 8.8% in readers of the UK dance music magazine Mixmag; modal frequency of use was monthly (Winstock, personal communication). In university students in Florida (where *S. divinorum* was legal at the time of the study), 11% of males and 4% of females reported a lifetime use (Khey et al., 2008). A similar study in California estimated last-year prevalence at 4.4% (Lange et al., 2008). Regression analysis in another US college sample showed users were most likely to be young white males with a high prevalence of cannabis use (Miller et al., 2009). Over half of respondents in an internet-based survey reported reduction or cessation of use in the previous 12 months, most commonly citing dislike of the subjective effects or a loss of interest in *S. divinorum* (Biglete et al., 2009). In this study, age of initiation was related to use function, with young adults reporting using for fun, whilst older adults cited 'spiritual' reasons (not defined by the authors, but see Saunders et al., 2000, and Wilber, 2006, for popular discussions). In retrospective surveys of the subjective effects of use, participants typically report a small number of lifetime uses ($n < 20$), and a range of hallucinogen/psychedelic-like experiences (Baggott et al., 2004). Interestingly, however, these are reported to be qualitatively distinct from those produced by serotonergic hallucinogens such as LSD and psilocin. For example, the derealization and physical impairment (similar to that produced by NMDA receptor antagonists) produced by *S. divinorum* at typical doses is thought to be unique, as this effect is only seen at relatively higher doses with other hallucinogens (Arthur, 2008; Ball, 2007; Dalgarno, 2007; González et al., 2006; Lange et al., 2010; Pendell, 1995). Data on the potential adverse effects and toxicity of *S. divinorum* are limited. Over 10 years, 37 cases were reported to the California Poison Control System after intentional exposure to *S. divinorum* (Vohra et al., 2011). Just under half of these were associated with ingestion of *S. divinorum* alone, and the most common symptoms were confusion or disorientation, hallucinations, dizziness, and gastrointestinal disturbances. All patients recovered after appropriate intervention. In rats, no significant effects were seen on heart rate, body temperature, or galvanic skin response after chronic salvinorin A administration, although an increase in pulse pressure was recorded (Mowry et al., 2003). Furthermore, toxicity was not apparent in mice after chronic administration of 400–6400 μg/kg (around 1–16 times the typical human dose) once daily over 2 weeks (Mowry et al., 2003).

One clinical case report described a 15-year-old male with a recent history of *S. divinorum* use presenting with paranoia, déjà vu and blunted affect shortly after self-administration of cannabis (Singh, 2007). An 18-year-old female was admitted to psychiatric services with acute onset of agitation, disorganization, and hallucinations shortly after smoking cannabis (Paulzen and Gründer, 2008). It transpired that her partner had added *S. divinorum* to the herbal cannabis smoking mixture. A 21-year-old man also presented with symptoms of acute psychosis and paranoia, including echolalia and psychomotor agitation (Przekop and Lee, 2009). Despite antipsychotic treatment the authors noted that the patient did not exhibit improvement at 4 months' follow-up. In all three cases, the authors exclusively attributed these symptoms to *S. divinorum* because of purported links between κ-opioid receptor agonist activity and changes in dopaminergic transmission, with psychomimetic symptomatology (Pfeiffer et al., 1986). However, with respect to this latter case, it should be noted that chronic psychotic episodes after hallucinogen use are rare (Strassman, 1984), and the authors provided no information on treatment adherence during this period. In contrast, daily low-dose self-medication for depression with orally administered *S. divinorum* leaves has been reported, apparently with the full remission of symptoms (Hanes, 2001).

Understanding of the behavioural pharmacology of salvinorin A is growing. A study investigating the human pharmacokinetics of smoked salvinorin A had to be abandoned after the two volunteers became too intoxicated to provide blood samples, although it appeared in urine up to 1.5 h after administration, suggesting rapid elimination (Pichini et al., 2005). In non-human primates, the elimination half-life of salvinorin A was 56.6 ± 24.8 minutes after a bolus intravenous (i.v.) administration that was predicted to have the same disposition as the smoked drug (Schmidt et al., 2005). Sex-dependent pharmacokinetics were also noted, suggesting the possibility of differences in pharmacology. Salvinorin A produced dose-dependent κ-opioid receptor agonist-like response after drug discrimination training with U69,593 in both rats and rhesus monkeys, supporting the role of this receptor in the production of behavioural/subjective effects (Baker et al., 2009; Butelman et al., 2004; Wilmore-Fordham, 2007). However, salvinorin A did not substitute for the 5-HT_{2A} receptor agonist hallucinogen DOM in rhesus monkeys (Li et al., 2008). As with other κ-opioid receptor agonists, administration of salvinorin A attenuated cocaine seeking in rats (Morani et al., 2009) and produced a conditioned place aversion in mice at high doses (1–3.2 mg/kg) (Zhang et al., 2005). This latter effect was similar to that produced by mescaline (Cappell and LeBlanc, 1971), but not LSD (Meehan and Schechter, 1998), and was associated with a decrease in dopamine concentration in the caudate putamen. However, in rats, 0.05–160 μg/kg subcutaneous (s.c.) salvinorin A produced a conditioned place preference, and 0.01–1 μg intracerebroventricular (i.c.v.) infusions were self administered (Braida et al., 2008). Place preference was also observed in zebra fish (Braida et al., 2007). These findings suggest that the rewarding effects of salvinorin A may be dose, species, and model specific. In mice, antinociception, sedation, and motor incoordination effects have been observed (Fantegrossi et al., 2005; McCurdy et al., 2006), and in the forced swim test rats treated with high doses of salvinorin A showed increased immobility and decreased swimming, suggesting pro-depressant like effects (Carlezon et al., 2006). However, at lower doses (0.25–2 mg/kg), rats exhibited both anxiolytic and antidepressant effects (Hanes, 2001), again suggesting behavioural effects are dose dependent (Braida et al., 2009).

Although not a new phenomenon (Hoffmann, 1980), the increased awareness of the use of *S. divinorum* has led to both public health and legislative concerns (Bücheler et al., 2005). Federal legislation against *S. divinorum* exists only in some

countries, and there is also legislation in some USA states, although at the time of writing the UK's Advisory Council on the Misuse of Drugs (ACMD) is considering providing recommendations for Government on its legal status. This concern has partly been driven by perceived ease of access to *S. divinorum* and other drugs through the internet and city centre retailers (Dennehy et al., 2005; Halpern and Pope, 2001; Hoover et al., 2008; Siemann et al., 2006), and also by popular representations of use in the media, particularly through new media such as the online YouTube video site (Lange et al., 2010). Other authors have suggested that such powerful, but legal, recreational drugs are popular as they allow intoxication without the need for otherwise law-abiding citizens to engage with criminal markets (Hammersley, 2010; Measham et al., 2010).

This study aimed to provide further clarification of the subjective effects of *S. divinorum*, use patterns, and experience of adverse effects in order to inform psychopharmacologically based public health discussions. The present study explored multidimensional attitudes regarding *S. divinorum* which provided a more complete cultural understanding than that reported by González et al. (2006). We were also interested in whether the legality of *S. divinorum*, and as a consequence relative ease of availability, was a motivating factor for use. Furthermore, considering the case reports cited above describing psychosis after acute administration, we analysed reporting of schizotypy in the sample to investigate whether *S. divinorum* users had increased risk of psychosis (Williams et al., 1996).

Methods

Subjects

Participants were recruited by advertisements posted on internet sites discussing *S. divinorum* and other substance use, online retailers, and social networking sites (Facebook, MySpace). Cards advertising the study were also provided to internet and 'head'/smart shops retailers in the North West of England to include with *S. divinorum* purchases. As prevalence is relatively low compared with other recreational drugs, convenience sampling was deemed appropriate for this research. The study was advertised as an investigation of the effects of *S. divinorum* and was only open to those who reported using *S. divinorum* at least once in their lifetime. All potential volunteers were provided with detailed information about the study and were assured that their responses would remain confidential. The ethics committee at Liverpool John Moores University gave their approval for this research study and all subjects were required to give informed consent after reading a description of the investigation.

Questionnaire design

Volunteers were required to complete a single online questionnaire hosted by Bristol Online Surveys (http://www.survey.bris.ac.uk/). The questionnaire asked for participant demographic information and a detailed history of use of a wide variety of substances. The time of survey submission and patterns of answers were inspected to reduce the chance that individuals had submitted more than one survey. The Severity of Dependence Scale (SDS) (Gossop et al., 1995) was included to assess dependence upon *S. divinorum*. Although this scale has not been previously validated for *S. divinorum* it was believed that this would provide important preliminary information on the likelihood of use disorders. Furthermore, the SDS yields robust assessments on a range of abused drugs. The next section requested information on *S. divinorum* purchasing patterns, including those formulations usually purchased, sources of purchases, and reasons for use (e.g. 'interest in drug-induced states of consciousness'; 'curiosity'). Participants were then asked to think about their most recent (representative) *S. divinorum* experiences (for example, length of experience, circumstances surrounding use), and were presented with a list of 31 statements that described typical subjective effects of classical hallucinogens and related drugs. Items were generated from earlier informal interviews with hallucinogen users, personal communications with colleagues, and also adapted from literature describing the acute and immediate recreational effects of *S. divinorum* (Albertson and Grubbs, 2009; Dalgarno, 2007; González et al., 2006). Further items were adapted from the Psychedelic Experience Questionnaire (Pahnke and Richards, 1966) and the ecstasy effect experiences questionnaire (Sumnall et al., 2006). Participants were asked to indicate how often they experienced each particular effect or event listed after taking *S. divinorum* by selecting a number along a five-point Likert scale. Finally, the questionnaire included the cognitive–perceptual subscale of the schizotypy personality questionnaire (SPQ) (Raine, 1991). In normal populations, the mean score of the subscale is 11.7 ± 7.4 (Raine, 1992).

Statistical analyses

Preliminary data screening reduced the number of scale variables included in subsequent analyses. Briefly, we identified and removed items with limited range (i.e. all points on the scale not used) and/or with high/low standard deviation. Other items were considered for removal if they yielded statistically significant skewness and kurtosis distribution scores, or if they did not significantly correlate at 1% or 5% significance levels, along with items correlating too highly with many other items to avoid multicollinearity. This resulted in the exclusion of two items ('On salvia I found it hard to take on ordinary social roles'; 'On salvia I thought more in images than in abstract thoughts'). The remaining variables were entered into a principal components analysis (PCA) with Scree plot criterion to determine the number of components to be entered into oblique direct oblimin rotation. Before final analysis of the extracted components, the anti-image matrix was examined to enable removal of partially correlated items. Factor-based scale scores were generated and subscales were explored as a function of use intention, patterns of drug use and demographics using a variety of statistical techniques. SPSS v18.0 was used for all analysis; significance was set at $p < 0.05$.

Results

In total, 209 people began the survey, and 155 completed it (74.2% completion rate). Reasons for non-completion

are unknown. Non-completers were equally likely as completers to be male, resident in the UK or USA, and report similar ages and drug use histories. Unfortunately not enough data were submitted to compare scale scores. Data from one participant who had completed the whole survey were excluded as deliberately misleading answers were provided. Of the 154 analysed datasets, 128 (83.1%) were from males and 26 (16.9%) females. The mean age of respondents was 24.7 ± 8.7 years, and 135 (87.7%) self reported their ethnicity as Caucasian. In total, 59 (38.3%) had completed at least an undergraduate university degree, with the majority of others reporting either completing further, or some higher education. The modal occupation was student ($n = 54$, 35.1%), and other respondents were either employed ($n = 67$, 43.5%) or unemployed ($n = 13$; 8.4%). The majority of respondents lived in the United States ($n = 92$, 59.7%), followed by the United Kingdom ($n = 29$; 18.8%).

Drug use history

Table 1 shows substance use histories. No one reported use of naloxone, which was included to help verify accuracy of reporting. After *S. divinorum*, the most frequently reported substances were alcohol, cannabis, tobacco, and psilocybin mushrooms. Almost three-quarters of respondents reported use of *S. divinorum* in the previous year (73.4%), suggesting just over one-quarter had either ceased or reduced their use after their initial use, and subjects estimated that they used it twice a month during regular use periods. On average, time since last use in those reporting use in the previous year was 10 days (range 1–30 days). The mean SDS score for *S. divinorum* in previous year users was 0.4 ± 1.4 (range 0–10); five respondents scored above 4, suggesting the presence of a use disorder.

S. divinorum *use history*

The age of first use of *S. divinorum* was 21.7 ± 7.9 years (range 13–65 years). It was most frequently obtained from 'head'/smart shops ($n = 85$), followed by online retailers ($n = 67$), friends and relatives ($n = 37$), cuttings from a live plant ($n = 15$), and from illegal drug dealers ($n = 2$). It was usually taken at home (74% of respondents) or outdoors (excluding music festivals) (20.8%). Of those who bought it from 'head'/smart shops, 84.6% reported that it was usually on clear display (as opposed to having to ask specifically for it). Table 2 shows the formulations usually purchased. Some 40 subjects (26%) reported that they used *S. divinorum* as an alternative to illegal drugs. Of these, 27.5% reported they did so because they did not wish to break the law; 27.5% because they wanted to try a new experience; 22.5% because they preferred natural products; 17.5% because it produced similar effects to illegal hallucinogens such as LSD and mushrooms; and 5% because it was considered easier to obtain than illegal drugs.

Table 1. Drug use characteristics in *Salvia divinorum* users. All values are mean ± SD

	% reporting ≥1 use in lifetime ($n = 154$)	% reporting use in previous year	Self-reported uses in typical month in previous year[1]	Days since last use[2]
Alcohol	95.5	89.6	7.7 ± 7.4	5.2 ± 6.5
Amphetamine sulphate	40.3	21.4	9.4 ± 10.9	7.1 ± 7.9
Anabolic steroids	2.6	1.3	6.5 ± 7.8	1.0 ± 0.0
BZP[3]	13.6	6.5	3.2 ± 4.7	10.3 ± 11.4
Cannabis	95.5	84.4	15.5 ± 11.4	4.9 ± 6.5
Cocaine (powder)	48.7	20.1	4.3 ± 6.2	11.3 ± 10.3
Cocaine (crack)	12.3	1.9	9.5 ± 0.7	4.0 ± 0.0
GHB[4]	8.4	1.9	4.0 ± 2.2	5.5 ± 2.1
Glue/solvents	9.1	1.9	2.3 ± 2.3	4.5 ± 0.7
Heroin	14.3	8.0	5.1 ± 5.5	8.2 ± 11.2
MDMA (Ecstasy)	63.6	39.0	1.9 ± 1.9	12.0 ± 8.8
Ketamine	28.6	12.3	2.6 ± 1.9	9.4 ± 9.2
LSD[5]	54.5	33.1	1.5 ± 1.3	12.3 ± 9.5
Methamphetamine	14.3	5.2	3.7 ± 3.9	15.0 ± 13.0
Mushrooms[6]	80.5	42.9	2.0 ± 2.9	14.2 ± 9.3
Amyl nitrate 'Poppers'	24.0	6.5	4.4 ± 7.7	11.5 ± 6.4
Salvia Divinorum	100.0	73.4	1.8 ± 1.9	10.0 ± 9.3
Spice[7]	20.3	16.2	3.8 ± 3.8	12.1 ± 11.8
TFMPP[8]	4.5	2.6	0.7 ± 0.5	20.0 ± 0.0
Tobacco	85.7	56.5	18.0 ± 12.8	4.0 ± 6.9
Tranquilisers[9]	33.8	16.9	–	10.3 ± 9.1
Sildenafil (Viagra)	9.7	8.0	–	6.0 ± 1.0

[1]In those who reported use in the previous year; [2]in those who reported use in the last month; [3]1-benzylpiperazine; [4]γ-hydroxybutyrate; [5]Lysergic Acid Diethylamide; [6]typically *Psilocybe Semilanceata*, *Psilocybe Cubensis*, and *Psilocybe Mexicana*; [7]*Spice* is the generic name of a smoking mixture consisting of synthetic cannabinoids added to a herbal substrate; [8]1-(3-(Trifluoromethyl)phenyl) piperazine; [9]any form of anxiolytic or hypnotic drug.

If *S. divinorum* was made illegal in their country, 72.1% reported that they would continue using it, and 79.9% would continue to use if a supply could be guaranteed. There was no difference in lifetime and last-year drug use prevalence between those who reported using *S. divinorum* as an alternative to illegal drugs and those who did not (data not shown). Of the sample, 60.4% thought that it was either important or extremely important to them that *S. divinorum* was legal, 13.6% thought it was either slightly or not at all important, and 26% neither important nor unimportant. A third (33.2%) of respondents reported taking other drugs at the same time (±1–2 h) as *S. divinorum*, including alcohol (13.7% of respondents); cannabis (33.2%); and other hallucinogens (6.6%).

Participants were asked to report *S. divinorum* use functions, differentiating between their first use, and more recent occasions (if different). These are shown in Table 3. There appeared to be changes in the proportion endorsing each use function as experience with *S. divinorum* increased. For example, whilst 13.6% reported use for personal 'psychotherapy' at initiation, this had increased to 61.1% at the most recent episode; conversely, endorsement of curiosity decreased from 82.5 to 29.2%.

Comparing use behaviours in young (<21 years, $n = 103$) versus adult (>21 years, $n = 51$) initiates, it was found that younger initiates were just as likely to use *S. divinorum* indoors (odds ratio (OR) = 0.44, CI = 0.17–1.15, $p = 0.08$), and to purchase from an online or 'head'/smart shops (OR = 1.59, CI = 0.75–3.37, $p = 0.23$) as older initiates. Examining use functions, younger initiates were much more likely to report using *S. divinorum* at both the first and most recent episode 'For fun' (OR = 7.01, CI = 3.16–15.59, $p < 0.001$; OR = 2.89, CI = 1.23–6.80, $p < 0.05$, respectively). Differences in the likelihood of endorsement of other use functions were non-significant (data not shown).

Respondents were asked to estimate the time course of their most recent *S. divinorum* experience. The total experience was estimated to last for 21.8 ± 25.2 min; initial effects after ingestion were felt after 1.3 ± 2.9 min; subsequent onset to peak subjective effects lasted for 2.3 ± 10.1 min, and lasted for 8.4 ± 8.7 min; *S. divinorum* effects took approximately 14.3 ± 24.5 min to subside, and after effects 52.7 ± 429.6 min (this large SD was attributed to one respondent who reported residual effects up to 80 h after administration).

A range of adverse effects was reported after administration of *S. divinorum*, including; excessively intense experience (reported by 51.9%); unexpected effects (46.1%); loss of control over the experience (42.2%); heaviness of head, like smoking too many cannabis joints (27.9%); unpleasant physical effects (27.3%); unreliable effects (27.3%); tiredness (24.7%); dizziness (22.1%); grogginess (21.4%); mental slowness (20.8%); physically exhaustion (17.5%); and unpleasant after effects (16.2%).

Participants were presented with a range of *S. divinorum*-related behaviours and first asked to rate acceptability and then to indicate whether they had ever undertaken it (Table 4). Subjects showed disapproval of a range of public and social use behaviours, especially those involving deception and social responsibilities.

Principal component analysis

The Kaiser–Meyer–Olkin measure of sampling adequacy was 0.797, indicating the solution was robust (Hutcheson and Sofroniouo, 1999). The Bartlett's test of sphericity was significant ($p < 0.001$), indicating the original correlation matrix was not an identity matrix. Items were removed from the solution if loadings were less than 0.40 on primary

Table 3. Endorsed Salvia use functions on first and recent occasions. Shown are percentages, totals >100% as participants could report more than one function

	% reporting	
Function	First use	Most recent use
As part of a personal 'psychotherapy'	13.6	61.1
Curiosity	82.5	29.2
For (self-defined) spiritual purposes	49.4	87.0
For fun	48.7	56.5
For social purposes	11.7	7.1
Interest in drug-induced states of consciousness	81.2	61.7
To enhance creativity	11.0	19.5
To enjoy music	5.8	17.8
To feel close to nature	11.7	23.4

Table 2. Preparations of Salvia usually purchased by the sample. Extracts (5–60×) refer to 'strength' of preparations sold by retailers, although no units of measurement are provided. For example 1× usually refers to the natural potency of the plant (~2.5 mg/g), whilst 10× would be ten times the potency of 1×. These 'doses' are often subjective and are also partly determined by the age and water weight of the plant (Wolowich et al., 2006; Vohra et al., 2011)

Extract	5×	10×	20×	40×	60×	Other
% ($n = 286$ mentions)	18.2	8.0	31.1	10.5	8.0	24.2
Dried leaf	28 g	56 g	100 g	200 g	Other	
($n = 66$)	54.5	21.2	3.0	3.0	18.3	
Tincture	2 mL	10 mL	Other			
($n = 19$)	42.1	47.3	10.6			
Other forms	Whole plants; cuttings; extraction using whole leaf and acetone; fresh leaf; extracted Salvinorin A; pre-rolled joints					

Table 4. Perceived acceptability of different types of Salvia use behaviours

Behaviour	Modal response (% reporting)	% reporting this activity
Using Salvia in public places	Strongly disagree (55.2%)	14.9
Posting videos of Salvia on YouTube	Strongly disagree (54.5%)	1.9
Giving someone else an unexpected dose (e.g. telling them it was cannabis)	Strongly disagree (91.6%)	1.3
Giving someone else an unexpectedly high dose	Strongly disagree (83.8%)	3.9
Having a hidden negative motive for giving it to someone else (e.g. to make them panic)	Strongly disagree (94.8%)	0.6
Having a neutral motive for giving it to someone else (e.g. so that they can experience the psychedelic effects)	Agree (37.0%)	32.5
Driving shortly after use	Strongly disagree (73.4%)	3.2
Combining Salvia with responsibilities (e.g. childcare, before going to work/college)	Strongly disagree (72.7%)	3.2
Selling it on at a profit	Neither agree nor disagree (36.4%)	5.8

Table 5. *Salvia divinorum* experiences questionnaire components. Survey respondents were requested to refer to their most recent use

Item	Item loading	Mean score (±SD)
1. Positive effects (Eigenvalue = 6.89; 22.24% of variance; α = 0.87)		31.7 (11.2)
On Salvia I felt that there were no boundaries between inner and outer reality	0.73	2.39 (1.53)
I had a noetic sense on Salvia; that is I instinctively understood the universe	0.67	1.96 (1.49)
When on Salvia I felt a personal identification with whatever I was looking at; a sense of unity	0.64	1.73 (1.43)
Salvia produced a sense of reverence in me	0.64	2.14 (1.39)
Salvia made me feel beyond or outside of time	0.63	3.14 (1.15)
I felt more connected to other people when I was on Salvia	0.58	1.23 (1.29)
I have the sense that in order to describe parts of the Salvia experience I would have to use statements that appear to be illogical, involving contradictions and paradoxes	0.58	2.90 (1.25)
On Salvia, wherever I looked was especially beautiful	0.56	1.73 (1.34)
I experienced variations in the passing of time	0.54	2.84 (1.24)
If I tried to smell something I could do so more vividly than when off Salvia	0.53	0.79 (1.09)
I felt that my consciousness/mind was located outside my physical body	0.5	2.32 (1.44)
Salvia made the temperature of things take on new qualities	0.49	1.62 (1.43)
Auditory images (mental images that I created in response to things that I hear) were more vivid when I was on Salvia	0.48	2.39 (1.36)
I felt changes in the perception of my size, weight, and posture when I was on Salvia	0.46	2.72 (1.36)
My memory for otherwise forgotten things was strong on Salvia	0.44	1.39 (1.36)
I felt that though I was still myself, at the same time I was also someone or something else	0.40	1.47(1.38)
2. Negative intoxication effects (Eigenvalue = 5.45; 17.59% of variance; α = 0.70)		20.4 (7.0)
I had a transcendental experience on Salvia. I felt detached from all problems, anxieties and human interactions	−.60*	2.31 (1.39)
When I had taken Salvia I felt an increased ease and enjoyment of talking to and understanding people	−.59*	1.05 (1.19)
When I was on Salvia I had strong feelings of caring or compassion for people who I was with	−.50*	1.34 (1.34)
On Salvia I could deliberately generate insights concerning myself, my personality, and my relationships with other people	−.43*	1.61 (1.44)
When I was on Salvia I found that I had problems remembering things	0.65	1.91 (1.54)
I got anxious when I was on Salvia	0.59	1.47 (1.38)
Salvia lowered my inhibitions so that I said and did things I'm normally too inhibited to do	0.56	0.87 (1.08)
I had difficulty focusing upon one thing at a time when I was on Salvia	0.51	1.77 (1.43)
After the Salvia high was over I became depressed or 'burned out'	0.47	0.57 (1.01)
Salvia gave me headaches	0.42	0.50 (0.94)
I experienced thoughts that I believed were not my own	0.40	1.77 (1.43)

*Note negative loading.

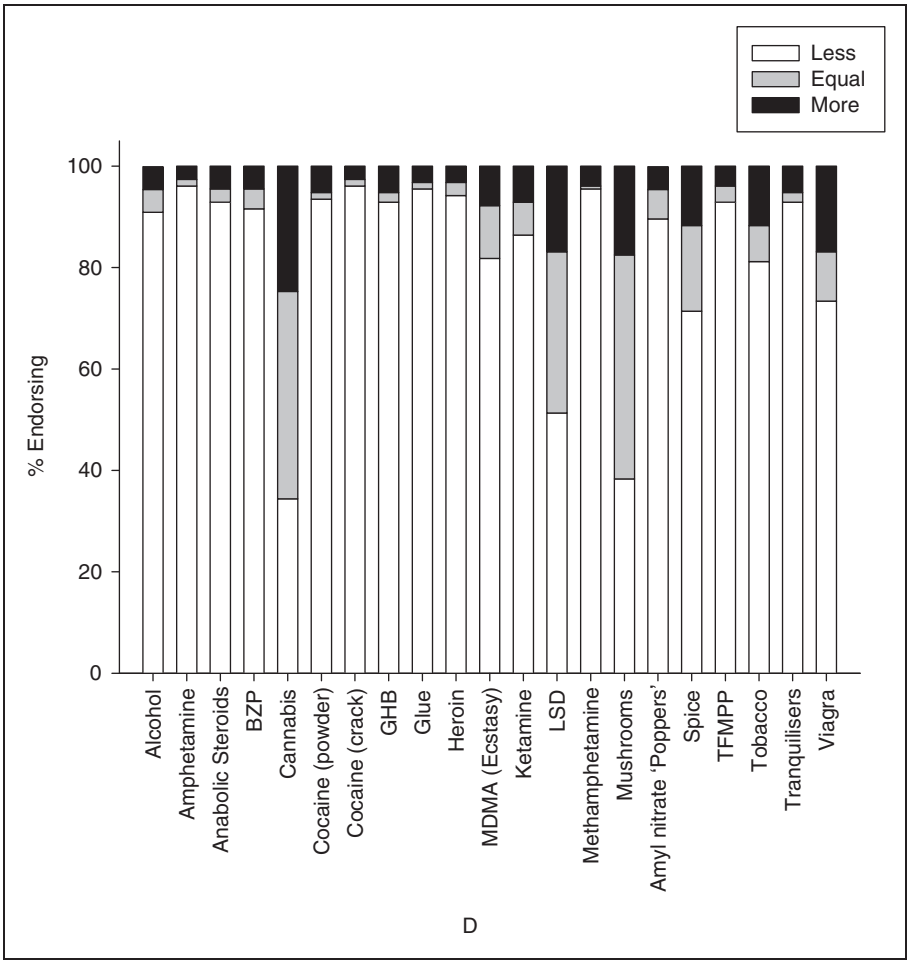

Figure 1. Perceived harmfulness of *Salvia divinorum* compared with other drugs. BZP, 1-benzylpiperazine; GHB, γ-hydroxybutyrate; LSD, Lysergic Acid Diethylamide; Mushrooms are typically *Psilocybe Semilanceata*, *Psilocybe Cubensis* and *Psilocybe Mexicana*; Spice is the generic name of a smoking mixture consisting of synthetic cannabinoids added to a herbal substrate; TFMPP, 1-(3-(Trifluoromethyl)phenyl) piperazine; tranquilisers are any form of anxiolytic or hypnotic drug.

components or greater than 0.40 on a secondary component. Rotation retained two components (29 items) accounting for 40% of the total item variance. This was confirmed by visual inspection of the Scree plot. *Positive effects* consisted of 17 items, and *Negative intoxication effects* consisted of 12 items (Table 5).

Backwards stepwise regression was used to identify predictors of positive and negative *S. divinorum* effect component scores. Predictors of positive effect scores ($r^2 = 0.245$, $p < 0.001$) were using *S. divinorum* outdoors ($\exp(\beta) = 0.234$, $p < 0.05$); younger age of initiation ($\exp(\beta) = -0.315$, $p < 0.05$); shorter time of *S. divinorum* effect onset ($\exp(\beta) = -0.252$, $p < 0.05$), and a greater length of time for acute effects to subside ($\exp(\beta) = 0.355$, $p < 0.01$). Predictors of negative effect scores ($r^2 = 0.232$, $p < 0.001$) were using *S. divinorum* indoors ($\exp(\beta) = 0.269$, $p < 0.05$); being of a younger age ($\exp(\beta) = -0.332$, $p < 0.05$), and reporting higher SPQ scores ($\exp(\beta) = 0.403$, $p < 0.001$).

Regarding the perceived harmfulness of *S. divinorum*, respondents were asked to compare the relative harmfulness of their own type and pattern of *S. divinorum* use with that of other drugs (Figure 1). *S. divinorum* was perceived to be less harmful than all drugs apart from cannabis (Class B under the UK Misuse of Drugs Act 1971 since 2009) and mushrooms (all forms of psilocin are Class A under the Misuse of UK Drugs Act 1971 since 2005), which were viewed as equally harmful.

Table 6. Scores on the cognitive–perceptual components of the schizotypy personality (SPQ) questionnaire

Odd beliefs or magical thinking	2.1 ± 2.4
Unusual perceptual experiences	2.8 ± 2.3
Ideas of reference	3.2 ± 2.6
Suspiciousness	1.9 ± 2.2
Total SPQ (cognitive–perceptual subscale)	9.9 ± 7.5

Finally, data from the SPQ questionnaire are shown in Table 6. As can be seen, the mean sample score was consistent with general population mean of 11.7, indicating that this population was not experiencing schizotypal symptoms. However, there were small but significant correlations

between *S. divinorum* effect component scores and *total* SPQ score (*Positive effects* $r^2 = 0.282$, $p < 0.001$; *negative effects* $r^2 = 0.187$, $p < 0.001$). There were no significant correlations between *S. divinorum* component scores and SPQ subscales, and there were no significant differences in subscale score between younger and older initiates (data not shown).

Discussion

This study investigated the use behaviours and subjective experiences of *S. divinorum* in healthy adult subjects. Participants reported a range of drug use histories and experiences with *S. divinorum*. Use of other serotonergic hallucinogens (LSD, psilocybin mushrooms) was high compared with general population estimates (Hoare, 2009), but similar to other studies of *S. divinorum* users (Albertson and Grubbs, 2009; González et al., 2006). Therefore it would be useful to determine whether this population represents a distinct drug-use typology using techniques such as latent class/profile analysis. Subjects also appeared to have a sense of social 'responsibility' regarding their use, suggesting the establishment of informal user group injunctive norms. These findings are important, as drug prevention and harm reduction advice is often delivered through social marketing techniques that rely on an understanding of the experiences and motivations of the target audience (Bennett and Henderson, 1999).

PCA of responses to the survey of *S. divinorum* effects revealed two main components. *Positive effects* comprised perceptual and cognitive effects, whilst *Negative effects* included items related to social withdrawal, mental confusion, amnesia, and anxiety. Future research will allow for refining and improving component scale reliability. As expected (Schmidt et al., 2005), the *S. divinorum* experience was typically short (<22 min in total; 8.4 minutes for the peak subjective effects) and the items with the highest mean scores were those concerning derealization/depersonalization, auditory hallucinations, and perceptual changes. Surprisingly, the questionnaire item relating to visual hallucinations was not retained in the PCA. Although the mean score was high (2.36 ± 1.43) and the modal category reported was '*very strongly*', it was the only item to load onto a component ($\alpha = 0.863$), suggesting that it was a common feature of intoxication and therefore was not suitable for differentiating between phenomenologies. The reported effects represented a hallucinogen-like profile accompanied by derealization, and a decreased ability to interact with the environment, and thus were in keeping with those of González et al. (2006), and Albertson and Grubbs (2009). However, because of the scale completion time required, unlike those authors we did not use the Addiction Research Center Inventory (ARCI) (Haertzen et al., 1963), Aussergewöhnliche Psychische Zustände (APZ) (Dittrich, 1996) or the Hallucinogen Rating Scale (HRS) (Strassman et al., 1994) in the present study. Interestingly, Albertson and Grubbs (2009) reported that in their sample the ARCI indicated *S. divinorum* was considered more marijuana-like than LSD-like; this was in contrast to the findings of González et al. (2006), but more in keeping with drug discrimination studies (Li et al., 2008). This discrepancy was probably a dose-related effect but also suggested that prior drug use history was important in determining which phenomena were attended to (Albertson's sample had less experience with hallucinogens). Furthermore, the ARCI–LSD scale is most sensitive to somatic and dysphoric drug effects and does not include complex hallucinogen-like phenomenology (Haertzen et al., 1963; Hill et al., 1963), and hence may not be appropriate for differentiating between subjective hallucinogen experiences. Additionally, the HRS has also only been previously validated with dimethyltryptamine (DMT) (Riba et al., 2001; Strassman et al., 1994), and so a combination of substance-specific scales and repertory grid analysis, based on personal construct theory, and analysed with multivariate statistics, may be one novel idiographic way of comparing detailed information on the subjective effects of different types of hallucinogens that does not rely entirely on the use of general questionnaires (Jankowicz, 2004).

In keeping with pre-clinical data showing that κ-opioid receptor agonists in general, and salvinorin A in particular, are less reinforcing than μ and δ receptor agonists (Shippenberg et al. 1987; Woods and Winger 1987; Young et al. 1984), we found that respondents did not report use disorders as measured by the SDS. Examining substance use histories, it was clear that while respondents reported use of a range of drugs, frequency of *S. divinorum* use was relatively low (around once a month during regular use periods), and around a quarter of subjects had ceased use. This could either indicate experimental use, or that users no longer desired the effects that the drug produced. In support of this latter assertion, only 44% of González et al.'s (2006) population of Spanish *S. divinorum* users reported that they would wish to take it regularly (*S. divinorum* was legal to possess or use in Spain at the time of their study). Like other hallucinogens, but unlike ketamine, *S. divinorum* therefore does not appear to pose a high risk of dependence (Chung and Martin, 2005; Fantegrossi et al., 2004; Kendler et al., 2000; Lankenau and Sanders, 2007; Stone et al., 2006, 2007).

A variety of adverse effects were endorsed by respondents, and these were in keeping with the findings of González et al. (2006). The most frequently cited of these related to qualitative elements of the drug experience rather than psychopathological or physiological complaints. Interestingly, the most frequently endorsed responses were 'excessively intense experience' and 'unexpected effects', which do not suggest toxicological overdose, but that the dissociative and hallucinogenic effects of the drug were greater than those produced by similar substances. This profile of effects is similar to that reported in the toxicological history published by Vohra et al. (2011). Harm reduction advice should build upon these concerns. Reviews of the adverse effects of other hallucinogens, for example, suggest that although rare, long-term psychiatric morbidity may be related to acute psychopathology (i.e. so called 'bad trips', typically manifesting as anxiety, paranoia and panic attack) (McCabe, 1977; Strassman, 1984). The way that *S. divinorum* is marketed by some retailers (e.g. flavoured with fruit extracts, described as 'horse killer', sold as incense to avoid medicinal regulations) suggests that some products are being targeted at inexperienced users. Inexperienced users should be counselled to avoid 'high strength' extracts, be informed that the effects of *S. divinorum*

may be dissimilar to LSD and psilocybin, and/or ensure that a trusted friend is available to offer support during the experience (Johnson et al., 2008). The variable quality of *S. divinorum* preparations (Wolowich et al., 2006) and the range of formulations reported being offered for sale also suggests that harm reduction initiatives would also benefit from routine forensic analysis of available products. Although we did not investigate it in detail, ethnopharmacological investigation suggests that oral administration of *S. divinorum*, in contrast to other routes such as smoking, produces a gradual onset of effects and a sustained plateau of intoxication (Siebert, 1994). Administration methods in 'industrialized' countries, including the use of leaf extracts (typically smoked), result in a much more rapid onset of drug effects, which may lead to an increased likelihood of experiencing negative effects (Pichini, et al., 2005). Harm reduction advice should therefore also counsel towards careful consideration of administration methods.

The study population reported levels of schizotypal symptomatology that were below those of the normal population (Raine 1992). It is often difficult to ascertain the relationship between substance use and psychopathological symptomatology. Association, causal, and indicator-variable explanations often hold true within the same population. Case reports have argued that acute manifestation of toxic psychosis is a direct result of *S. divinorum* use (Singh, 2007), and clinical administration of κ-opioid receptor agonists are known to produce psychotomimesis in humans (Dykstra et al., 1997; Pfeiffer et al., 1986; Walsh et al., 2001). However, the number of case reports in the literature is small, and the findings in this sample do not support the suggestion that negative symptomatology routinely extends beyond periods of intoxication. Psychopathology might also be a function of route of *S. divinorum* administration. It is also interesting to consider whether some symptoms that would otherwise be considered psychopathological by clinicians are in fact desirable to hallucinogen users. Precedents have been set with drugs such as LSD and ketamine, which were extensively investigated as psychotomimetics, but which subsequently showed popularity in recreational pharmacopeia despite, or even because of, phenomenological overlap between 'negative' desirable effects (Jansen, 2001; Lee and Shlain, 1992). In keeping with findings in cannabis users (Barkus et al., 2006), higher negative *S. divinorum* effect scores were associated with greater total SPQ score. In cannabis-using samples, those with high psychosis vulnerability were more likely than low scorers to report unusual perceptual experiences and thoughts following use (Barkus and Lewis, 2008; Verdoux et al., 2003). The nature of the subjective experience of *S. divinorum*, however, means that users might actively desire unusual perceptual experiences (as supported by the use functions reported in the present study), which would also lead to high SPQ scores. It is uncertain whether those with higher psychosis proneness may seek out *S. divinorum*, and so it will be important to determine whether these individuals are also more likely to experience acute psychotic episodes (Ferdinand et al., 2005).

Subjects expressed concerns about the legal status of *S. divinorum*. Although often considered primarily a criminal justice or clinical matter, it is important that psychopharmacological perspectives are also included in legislative decision making (see for example, Nutt, 2009). Around a quarter of participants reported using *S. divinorum* as an alternative to illegal drugs, but only 27.5% of these reported doing so to avoid breaking the law. Furthermore, only 5% used *S. divinorum* because it was easier to obtain than illegal drugs, and the majority of participants reported that they would continue to use *S. divinorum* even if it was made illegal. This may have been partly related to the perceived low level of harm that users associated with *S. divinorum*. Taken together, these data suggest that the primary driver of *S. divinorum* use is pursuit of altered states of consciousness, and that legal controls would do little to dissuade existing users from purchasing it (Siegel, 1989). However, the current sample consisted of experienced hallucinogen users who most frequently bought *S. divinorum* from 'head' shops and online retailers; proscriptive legislation might lead determined individuals to purchase the drug from illegal drug sellers, exposing them to other illicit products (Hammersley, 2010).

One finding worthy of comment was that use functions appeared to change as users became more experienced with using the drug. Interestingly, personal 'psychotherapy', spiritual purposes, enhancement of creativity, and feeling close to nature were more frequently present in the most recent use than in first use. These dimensions were more prominent than more mundane ones (e.g. curiosity, fun, enjoy music). Our population may therefore represent a subset of drug users who seek specific kind of drugs for spiritual and self-actualization needs. Interestingly, even if used with no religious setting (*cf* quasi Christian uses of ayahuasca; Labate et al., 2008), *S. divinorum* was still associated with spiritual purposes. Although often reported in surveys of drug users (e.g. Riley and Blackman, 2008; Sussman et al., 2006), obtaining a precise description of how study populations experience and define spirituality is difficult, and may either represent a cultural artefact (e.g. Leary et al., 1964; Masters and Houston, 2000) or be occasioned by drug use (e.g. Griffiths et al., 2008; Smith, 2000).

The present study suffers from several weaknesses common to many investigations of drugs of abuse (e.g. the use of a convenience sample, self-selection bias, etc.) (Cole et al., 2002), although a few are particularly pertinent. First, we relied on retrospective drug use histories, and so were unable to forensically examine *S. divinorum* materials ingested. As discussed elsewhere, purchased *S. divinorum* may be subpotent and contain adulterants (Wolowich et al., 2006); hence we did not attempt to associate *S. divinorum* effects with the amount reported to have been ingested. This confound could be overcome with administration of known doses of *S. divinorum* plant material or salvinorin A in the clinic. Although there have been insufficient human safety studies conducted (cf Pichini et al., 2005), numerous ethnopharmacological reports have described the use of *S. divinorum* without apparent adverse outcomes (e.g. Ott, 1995; Siebert, 1994; Valdés et al., 1983) and so this should provide a useful avenue of research. Second, we also relied on retrospective recall of subjective effects. Memory of phenomena may therefore have been biased by subsequent experiences (both drug and non-drug) and selective attention

to particular drug effects. Our similar work with ecstasy suggests that recall bias was not a major confound in recalling subjective drug states (Sumnall et al., 2006), and convergence between the findings of this study and others (e.g. González et al., 2006) indicates that our findings are robust. Although we attempted to assess schizotypy, because of space and time constraints, we only included certain subcomponents from the schizotypy personality questionnaire. In follow-up work it will therefore be important to include other dimensions and multiple assessments to establish the veracity of the current findings. Finally, around 25% of the participants who started the online study did not complete it. It is uncertain why non-completions occurred, but they may be partly attributable to respondents navigating through the pages to observe the survey questions out of personal interest in the research, or boredom. This is an inevitable weakness of online convenience sampling techniques such as the one employed for this study, as in order to increase response rate, survey materials cannot be password protected. Analysis did show, however, that non-completers did not differ from completers on any demographic variables.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

Albertson D and Grubbs LE (2009) Subjective effects of *Salvia divinorum*: LSD- or marijuana-like? *J Psychoactive Drugs* 41: 213–217.

Arthur JD (2008) *Peopled darkness: Perceptual transformation through Salvia divinorum*. Privately published: iUniverse.com.

Baggott MJ, Erowid E, Erowid F and Mendelson JE (2004) Use of *Salvia divinorum*, an unscheduled hallucinogenic plant: a web-based survey of 500 users. *Clin Pharmacol Ther* 75: 72.

Baker LE, Panos JJ, Killinger BA, Peet MM, Bell LM, Haliw LA, et al. (2009) Comparison of the discriminative stimulus effects of salvinorin A and its derivatives to U69,593 and U50,488 in rats. *Psychopharmacology* 203: 203–211.

Ball MW (2007) *Sage Spirit – Salvia divinorum and the Entheogenic Experience*. Oregon, USA: Kyandara Publishing.

Barkus EJ and Lewis S (2008) Schizotypy and psychosis-like experiences from recreational cannabis in a non-clinical sample. *Psychol Med* 38: 1267–1276.

Barkus EJ, Stirling J, Hopkins RS and Lewis S (2006) Cannabis-induced psychosis-like experiences are associated with high schizotypy. *Psychopathology* 39: 175–178.

Beguin C, Duncan KK, Munro TA, Ho DM, Xu W, Liu-Chen LY, et al. (2009) Modification of the furan ring of salvinorin A: Identification of a selective partial agonist at the kappa opioid receptor. *Bioorg Med Chem* 17: 1370–1380.

Beguin C, Potter DN, DiNieri JA, Munro TA, Richards MR, Paine TA, et al. (2008) N-methylacetamide analog of salvinorin A: A highly potent and selective kappa-opioid receptor agonist with oral efficacy. *J Pharmacol Exp Ther* 324: 188–195.

Beguin C, Richards MR, Li JG, Wang YL, Xu W, Liu-Chen LY, et al. (2006) Synthesis and in vitro evaluation of salvinorin A analogues: Effect of configuration at C(2) and substitution at C(18). *Bioorg Med Chem Lett* 16: 4679–4685.

Bennett A and Henderson S (1999) *Using social marketing to promote and protect drug users' health. Executive Summary no 66*. London: The Centre for Research on Drugs and Health Behaviour.

Bigham AK, Munro TA, Rizzacasa MA and Robins-Browne RM (2003) Divinatorins A–C, new neoclerodane diterpenoids from the controlled sage *Salvia divinorum*. *J Nat Prod* 66: 1242–1244.

Biglete SA, Lai EP, Lee DY, Nyi PP, Torrecer GI and Anderson IB (2009) Influence of age on *Salvia divinorum* abuse: Results of an internet survey. *Clin Toxicol* 47: A51.

Braida D, Capurro V, Zani A, Rubino T, Vigano D, Parolaro D, et al. (2009) Potential anxiolytic- and antidepressant-like effects of salvinorin A, the main active ingredient of *Salvia divinorum*, in rodents. *Br J Pharmacol* 157: 844–853.

Braida D, Limonta V, Capurro V, Fadda P, Rubino T, Mascia P, et al. (2008) Involvement of κ-opioid and endocannabinoid system on salvinorin A-induced reward. *Biol Psychiatry* 63: 286–292.

Braida D, Limonta V, Pegorini S, Zani A, Guerini-Rocco C, Gori E, et al. (2007) Hallucinatory and rewarding effect of salvinorin A in zebrafish: κ-opioid and CB1-cannabinnoid receptor involvement. *Psychopharmacology* 190: 441–448.

Bücheler R, Gleiter CH, Schwoerer P and Gaertner I (2005) Use on nonprohibited hallucinogenic plants: Increasing relevance for public health. *Pharmacopsychiatry* 38: 1–5.

Butelman ER, Harris TJ and Kreek MJ (2004) The plant-derived hallucinogen, salvinorin A, produces κ-opioid agonist-like discriminative effects in rhesus monkeys. *Psychopharmacology* 172: 220–224.

Butelman ER, Mandau M, Tidgewell K, Prisinzano TE, Yuferov V and Kreek MJ (2007) Effects of salvinorin A, a κ-opioid hallucinogen, on a neuroendocrine biomarker assay in nonhuman primates with high κ-receptor homology to humans. *J Pharmacol Exp Ther* 320: 300–306.

Capasso R, Borrelli F, Capasso F, Siebert DJ, Stewart DJ, Zjawiony JK, et al. (2006) The hallucinogenic herb *Salvia divinorum* and its active ingredient salvinorin A inhibit enteric cholinergic transmission in the guinea-pig ileum. *Neurogastroenterol Motil* 18: 69–75.

Cappell H and LeBlanc AE (1971) Conditioned aversion to saccharin by single administration of mescaline and d-amphetamine. *Psychopharmacologia* 98: 352–356.

Carlezon WA, Beguin C, DiNieri JA, Baumann MH, Richards MR, Todtenkopf MS, et al. (2006) Depressive like effects of the kappa-opioid receptor agonist salvinorin A on behavior and neurochemistry in rats. *J Pharmacol Exp Ther* 320: 300–306.

Chung T and Martin CS (2005) Classification and short-term course of DSM-IV cannabis, hallucinogen, cocaine, and opioid disorders in treated adolescents. *J Consult Clin Psychol* 73: 995–1004.

Cole JC, Sumnall HR and Grob CS (2002) Sorted: ecstasy facts and fiction. *Psychologist* 15: 464–474.

Dalgarno P (2007) Subjective effects of *Salvia divinorum*. *J Psychoactive Drugs* 39: 143–149.

Dennehy CE, Tsourounis C and Miller AE (2005) Evaluation of herbal dietary supplements marketed on the internet for recreational use. *Ann Pharmacother* 39: 1634–1639.

Dittrich A (1996) *Ätiologie-unabhängige Strukturen veränderter Wachbewußtseinszustände*. Berlin: Verlag und Vertrieb.

Dykstra LA, Preston KL and Bigelow GE (1997) Discriminative stimulus and subjective effects of opioids with mu and kappa activity: Data from laboratory animals and human subjects. *Psychopharmacology* 130: 14–27.

Fantegrossi WE, Kugle KM, Valdes L, Koreeda M and Woods JH (2005) Kappa-opioid receptor-mediated effects of the plant-derived hallucinogen salvinorin A, on inverted screen performance in the mouse. *Behav Pharmacol* 16: 627–633.

Fantegrossi WE, Woods JH and Winger G (2004) Transient reinforcing effects of phenylisopropylamine and indolealkylamine hallucinogens in rhesus monkeys. *Behav Pharmacol* 15: 149–157.

Ferdinand RF, Sondeijker F, van der Ende J, Selten JP, Huizink A and Verhulst FC (2005) Cannabis use predicts future psychotic symptoms, and vice versa. *Addiction* 100: 612–618.

González D, Riba J, Bouso JC, Gomez-Jarabo G and Barbanoj MJ (2006) Pattern of use and subjective effects of *Salvia divinorum* among recreational users. *Drug Alcohol Depend* 85: 157–162.

Gossop M, Darke S, Griffiths P, Hando J, Powis B, Hall W, et al. (1995) The Severity of Dependence Scale (SDS): psychometric properties of the SDS in English and Australian samples of heroin, cocaine and amphetamine users. *Addiction* 90: 607–614.

Griffiths RR, Richards WA, Johnson MW, McCann UD and Jesse R (2008) Mystical-type experiences occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later. *J Psychopharmacol* 22: 621–632.

Grilli M, Neri E, Zappettini S, Massa F, Bisio A, Romussi G, et al. (2009) Salvinorin A exerts opposite presynaptic controls on neurotransmitter exocytosis from mouse brain nerve terminals. *Neuropharmacology* 57: 523–530.

Haertzen CA, Hill HE and Belleville RE (1963) Development of the Addiction Research Center Inventory (ARCI): selection of items that are sensitive to the effects of various drugs. *Psychopharmacologia* 4: 155–166.

Halpern JH and Pope HG (2001) Hallucinogens on the Internet: A vast new source of underground drug information. *Am J Psychiatry* 158: 481–483.

Hammersley R (2010) Dangers of banning Spice and the synthetic cannabinoid agonists. *Addiction* 105: 373.

Hanes KR (2001) Antidepressant effects of the herb *Salvia divinorum*: a case report. *J Clin Psychopharmacol* 21: 634–635.

Harding WW, Tidgewell K, Schmidt M, Shah K, Dersch CM, Snyder J, et al. (2005) Salvinicins A and B, new neoclerodane diterpenes from Salvia divinorum. *Org Lett* 7: 3017–3020.

Hill HE, Haertzen CA, Wolback AB and Miner EJ (1963) The Addiction Research Center Inventory: Appendix I. Items comprising empirical scales for seven drugs II. Items which do not differentiate placebo from any drug condition. *Psychopharmaeologia* 4: 184–205.

Hoare J (2009) *Drug Misuse Declared: Findings from the 2008/09 British Crime Survey England and Wales*. London: Home Office.

Hoffmann A (1980) *LSD, My Problem Child*. New York: McGraw-Hill.

Hoover V, Marlowe DB, Patapis NS, Festinger DS and Forman RF (2008) Internet access to Salvia divinorum: Implications for policy, prevention and treatment. *J Subst Abuse Treat* 35: 22–27.

Hutcheson G and Sofroniouo N (1999) *The Multivariate Social Scientist*. London: Sage.

Jankowicz D (2004) *The Easy Guide to Repertory Grids*. Chichester: Wiley.

Jansen K (2001) *Ketamine: Dreams and Realities*. Sarasota, Florida: MAPS.

Johnson MW, Richards WA and Griffiths RR (2008) Human hallucinogen research: Guidelines for safety. *J Psychopharmacol* 22: 603–620.

Kendler KS, Karkowski LM, Neale MC and Prescott CA (2000) Illicit psychoactive substance use, heavy use, abuse, and dependence in a US population-based sample of male twins. *Arch Gen Psychiatry* 57: 261–269.

Khey DN, Miller BL and Griffin OH (2008) Salvia Divinorum use among a college student sample. *J Drug Educ* 38: 297–306.

Labate BC, de Rose IS and dos Santos RG (2008) *Ayahuasca Religions: A Comprehensive Bibliography and Critical Essays*. Sarasota: MAPS Publications.

Lange JE, Daniel J, Homer K, Reed MB and Clapp JD (2010) Salvia divinorum: Effects and use among YouTube users. *Drug Alcohol Depend* 108: 138–140.

Lange JE, Reed MB, Ketchie Croff JM and Clapp JD (2008) College student use of Salvia divinorum. *J Drug Alcohol Depend* 94: 263–266.

Lankenau SE and Sanders B (2007) Patterns of ketamine use among young injection drug users. *J Psychoactive Drugs* 39: 21–29.

Leary T, Metzner R and Alpert R (1964) *The psychedelic experience: a manual based on the 'Tibetan book of the dead'*. New Hyde Park (NY): University Books.

Lee DYW, Ma ZZ, Liu-Chen LY, Wang YL, Chen Y, Carlezon WA, et al. (2005) New neoclerodane diterpenoids isolated from the leaves of Salvia divinorum and their binding affinities for human kappa opioid receptors. *Bioorg Med Chem* 13: 5635–5639.

Lee MA and Shlain B (1992) *Acid Dreams: The complete social history of LSD, the CIA, The sixties, and beyond*. New York: Grove/Atlantic.

Li J, Rice KC and France CP (2008) Discriminative stimulus effects of 1-(2,5-dimethoxy-4-methyl)-2-aminopropane in rhesus monkeys. *J Pharmacol Exp Ther* 324: 827–833.

Masters R and Houston J (2000) *The Varieties of Psychedelic Experience*. Vermont: Park Street Press.

McCabe OL (1977) Psychedelic drug crises: toxicity and therapeutics. *J Psychedelic Drugs* 9: 107–121.

McCurdy CR, Sufka KJ, Smith GH, Warnick JE and Nieto M (2006) Antinociceptive profile of salvinorin A, a structurally unique kappa opioid receptor agonist. *Pharmacol Biochem Behav* 83: 109–113.

Measham F, Moore K, Newcombe R and Welch Z (2010) Tweaking, Bombing, Dabbing and Stockpiling: The emergence of mephedrone and the perversity of prohibition. *Drugs Alcohol Today* 10: 14–21.

Meehan SM and Schechter MD (1998) LSD produces conditioned place preference in male but not female fawn hooded rats. *Pharmacol Biochem Behav* 53: 105–108.

Miller BL, Griffin OH, Gibson CL and Khey DN (2009) Trippin' on Sally D: Exploring Predictors of *Salvia Divinorum* Experimentation. *J Crim Justice* 37: 396–403.

Morani AS, Kivell B, Prisinzano TE and Schenk S (2009) Effect of kappa-opioid receptor agonists U69593, U50488, spiradoline and salvinorin A on cocaine-induced drug-seeking in rats. *Pharmacol Biochem Behav* 94: 244–249.

Mowry M, Mosher M and Briner W (2003) Acute physiologic and chronic histologic changes in rats and mice exposed to the unique hallucinogen salvinorin A. *J Psychoactive Drugs* 35: 379–382.

Munro TA and Rizzacasa MA (2003) Salvinorins D-F, new neoclerodane diterpenoids from Salvia divinorum, and an improved method for the isolation of salvinorin A. *J Nat Prod* 66: 703–705.

Nutt DJ (2009) Equasy – An overlooked addiction with implications for the current debate on drug harms. *J Psychopharmacol* 23: 3–5.

Ortega A, Blount JF and Manchand PS (1982) Salvinorin, a new *trans*-Neoclerodance Diterpene from Salvia divinorum (Labiatae). *J Chem Soc Perkin Trans I* 2505–2508.

Ott J (1995) Ethnopharmacognosy and human pharmacology of Salvia divinorum and salvinorin A. *Curare* 18: 103–129.

Pahnke W and Richards W (1966) Implications of LSD and experimental mysticism. *J Relig Health* 5: 175–208.

Paulzen M and Gründer G (2008) Toxic psychosis after intake of the hallucinogen Salvinorin A. *J Clin Psychiatry* 69: 1501–1502.

Pendell D (1995) *Pharmako/Poeia: Plant Powers, Poisons, and Herbcraft*. San Francisco: Mercury House.

Pfeiffer A, Brantl V, Herz L and Emrich HM (1986) Psychotomimesis mediated by κ opiate receptors. *Science* 233: 774–776.

Pichini S, Abanades S, Farre M, Pellegrini M, Marchei E, Pacifici R, et al. (2005) Quantification of the plant-derived hallucinogen salvinorin A in conventional and non-conventional biological fluids by gas chromatography/mass spectrometry after Salvia divinorum smoking. *Rapid Commun Mass Spectrom* 19: 1649–1656.

Przekop P and Lee T (2009) Persistent psychosis associated with Salvia divinorum use. *Am J Psychiatry* 166: 832.

Raine A (1991) The SPQ: A scale for the assessment of schizotypal personality based on DSM-III-R criteria. *Schizophr Bull* 17: 556–564.

Raine A (1992) Sex differences in schizotypal personality in a non-clinical population. *J Abnorm Psychol* 101: 361–364.

Riba J, Rodriguez-Fornells A, Strassman RJ and Barbanoj MJ (2001) Psychometric assessment of the Hallucinogen Rating Scale. *Drug Alcohol Depend* 62: 215–223.

Riley SCE and Blackman G (2008) Between prohibitions: Patterns and meanings of magic mushroom use in the UK. *Subst Use Misuse* 43: 55–71.

Roth BL, Baner K, Westkaemper R, Siebert D, Rice KC, Steinberg S, et al. (2002) Salvinorin A: A potent naturally occurring non-nitrogenous kappa opioid selective agonist. *Proc Natl Acad Sci* 99: 11934–11939.

SAMHSA (Substance Abuse and Mental Health Services Administration) Office of Applied Studies. (2008) *The NSDUH Report – Use of Specific Hallucinogens: 2006*. Rockville, MD: SAMHSA.

Saunders N, Saunders A and Pauli M (2000) *In Search of the Ultimate High: Spiritual Experience through Psychoactives*. London: Rider Books.

Schmidt MD, Schmidt MS, Butelman ER, Harding WW, Tidgewell K, Murry DJ, et al. (2005) Pharmacokinetics of the plant-derived κ-opioid hallucinogen salvinorin A in nonhuman primates. *Synapse* 58: 208–210.

Shippenberg TS, Bals-Kubik R and Herz A (1987) Motivational properties of opioids: Evidence that an activation of delta-receptors mediates reinforcement processes. *Brain Res* 436: 234–239.

Shirota O, Nagamatsu K and Sekita S (2006) Neo-clerodane diterpenes from the hallucinogenic sage Salvia divinorum. *J Nat Prod* 69: 1782–1786.

Siebert DJ (1994) Salvia divinorum and salvinorin A: New pharmacologic findings. *J Ethnopharmacol* 43: 53–56.

Siegel RK (1989) *Intoxication: Life in Pursuit of Artificial Paradise*. London: Penguin Books.

Siemann H, Specka M, Schifano F, Deluca P and Scherbaum N (2006) Salvia divinorum – Präsenz einer neuen Droge im Internet. *Gesundheitswesen* 68: 323–327.

Singh S (2007) Adolescent salvia substance abuse. *Addiction* 102: 823–824.

Smith H (2000) *Cleansing the Doors of Perception. The Religious Significance of Entheogens*. New York: Tarcher.

Stone AL, O'Brien MS, De la Torre A and Anthony JC (2007) Who is becoming hallucinogen dependent soon after hallucinogen use starts? *Drug Alcohol Depend* 87: 153–163.

Stone AL, Storr CL and Anthony JC (2006) Evidence for a hallucinogen dependence syndrome developing soon after onset of hallucinogen use during adolescence. *Int J Methods Psychiatr Res* 15: 116–130.

Strassman RJ (1984) Adverse reactions to psychedelic drugs: A review of the literature. *J Nerv Ment Dis* 172: 577–595.

Strassman RJ, Qualls CR, Uhlenhuth EH and Kellner R (1994) Dose-response study of N, N-dimethyltryptamine in humans. II. Subjective effects and preliminary results of a new rating scale. *Arch Gen Psychiatry* 51: 98–108.

Sumnall HR, Cole JC and Jerome L (2006) The varieties of ecstatic experience: an exploration of the subjective experiences of ecstasy. *J Psychopharmacol* 20: 670–682.

Sussman S, Skara S, Rodriguez Y and Pokhrel P (2006) Non drug use- and drug use-specific spirituality as one-year predictors of drug use among high-risk youth. *Subst Use Misuse* 41: 1801–1816.

Valdés LJ III, Butler WM, Hatfield GM, Paul AG and Koreeda M (1984) Divinorin A, a psychotropic terpenoid, and Divinorin B from the hallucinogenic Mexican mint *Salvia divinorum*. *J Org Chem* 49: 4716–4720.

Valdés LJ III, Chang HM, Visger DC and Koreeda M (2001) Salvinorin C, a new neoclerodane diterpene from a bioactive fraction of the hallucinogenic Mexican mint Salvia divinorum. *Org Lett* 3: 3935–3937.

Valdés LJ III, Díaz JL and Paul AG (1983) Ethnopharmacology of ska María Pastora (Salvia divinorum, Epling and Játiva-M). *J Ethnopharmacol* 7: 287–312.

Verdoux H, Gindre C, Sorbara F, Tournier M and Swendsen JD (2003) Effects of cannabis and psychosis vulnerability in daily life: an experience sampling test study. *Psychol Med* 33: 23–32.

Vohra R, Seefeld A, Cantrell FL and Clark RF (2011) *Salvia divinorum:* exposures reported to a statewide poison control system over 10 years. *J Emerg Med* 40: 643–650.

Walsh SL, Strain EC, Abreu ME and Bigelow GE (2001) Enadoline, a selective kappa opioid agonist: comparison with butorphanol and hydromorphone in humans. *Psychopharmacology* 157: 151–162.

Wang Y, Chen Y, Xu W, Lee DYW, Ma Z, Rawls SM, et al. (2008) 2-Methoxymethyl-salvinorin B is a potent κ opioid receptor agonist with longer action in vivo than salvinorin A. *J Pharmacol Exp Ther* 324: 1073–1083.

Wilber K (2006) *Integral Spirituality*. Boston: Shambhala Publications Inc.

Williams JH, Wellman JN and Rawlins JNP (1996) Cannabis use correlates with schizotypy in healthy people. *Addiction* 91: 869–877.

Wilmore-Fordham CB (2007) The hallucinogen derived from Salvia divinorum, salvinorin A, has k-opioid agonist discriminative stimulus effects in rats. *Neuropharmacology* 53: 481–486.

Wolowich WR, Perkins AM and Cienki JJ (2006) Analysis of the psychoactive Terpenoid salvinorin A content in five Salvia divinorum herbal products. *Pharmacotherapy* 26: 1268–1272.

Woods JH and Winger G (1987) Opioids, receptors, and abuse liability. In: Meltzer HY (ed.) *Psychopharmacology: The Third Generation of Progress*. New York: Raven Press, 1555–1564.

Young WS III, Alheid GF and Heimer L (1984) The ventral pallidal projection to the mediodorsal thalamus: a study with fluorescent retrograde tracers and immunohistofluorescence. *J Neurosci* 4: 1626–1638.

Zhang Y, Butelman ER, Schlussman SD, Ho A and Kreek MJ (2005) Effects of the plant-derived hallucinogen salvinorin A on basal dopamine levels in the caudate putamen and in a conditioned place aversion assay in mice: agonist actions at kappa opioid receptors. *Psychopharmacology* 179: 551–558.